Thrombectomy in high-Risk Pulmonary Embolism - Device versus thrombolysis Netherlands: TORPEDO-NL

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To determine whether CDT in high-risk PE relative to systemic thrombolysis is:- more effective and safer in terms of a reduction of the composite endpoint on all-cause mortality and adverse events defined as treatment failure, major&...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Embolism and thrombosis
Study type	Interventional research previously applied in human subjects

Summary

ID

NL-OMON57197

Source
ToetsingOnline

Brief title
TORPEDO-NL-Study

Condition

- Embolism and thrombosis

Synonym
pulmonary embolism, clotting in the lung

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum

Source(s) of monetary or material Support: ZIN/ZonMW

Intervention

- Medical device

Keyword: High risk Pulmonary Embolism, Thrombectomy, Thrombolysis

Explanation

N.a.

Outcome measures

Primary outcome

The primary outcome is the 30-day composite incidence of the binary endpoints
of:
1) all-cause mortality
2) treatment failure
3) major bleeding
4) and all-cause stroke

Secondary outcome

The secondary endpoints are:
- Survival at day 7 and day 30
- Treatment failure at day 7 and day 30
- All-cause mortality at day 7, day 30 and day 90
- All-cause stroke at day 7 and day 30
- The composite incidence of the binary endpoints of all-cause mortality,
treatment failure, major bleeding and all-cause stroke at day 7
- Desirability of Outcome Ranking (DOOR) at day 722
- BARC3b and BARC3c bleeding, at day 7 and day 30
- ISTH major and non-major clinically relevant bleeding at day 7 and day 30
- Oxygen supplementation (LO2/min) at 48 hours
- Length of stay (days) at the ICU and in hospital at day 30
- Quality of life, functional status and symptom burden symptom burden at day 7
and after 3, 6, 9 and 12 months according to the ICHOM-VTE set
- Cost-effectiveness analysis with a time horizon of one year and budget
impact analysis

Study description

Background summary

Patients with high-risk pulmonary embolism (PE) require immediate reperfusion therapy on top of anticoagulation. The standard reperfusion treatment in these patients is full-dose systemic thrombolysis. This carries a significant risk of major bleeding (10-25%) and intracranial haemorrhage (ICH, 3%). Catheter-directed thrombectomy (CDT) is a promising alternative to systemic thrombolysis with a more direct effect on reducing pulmonary artery clot burden and very likely a better safety profile. Randomized trials evaluating the

safety and efficacy of CDT in high-risk patients are currently unavailable. We hypothesize that in high-risk PE patients, CDT is superior to the current standard of systemic thrombolysis in terms of mortality and adverse events, i.e., is associated with a lower composite incidence of all-cause mortality, treatment failure, major bleeding and all-cause stroke. We also hypothesize that CDT will lead to a shorter length of stay (LOS) at the intensive care unit (ICU) and in-hospital, faster recovery, and better long-term quality of life (QoL).

Study objective

To determine whether CDT in high-risk PE relative to systemic thrombolysis is:
- more effective and safer in terms of a reduction of the composite endpoint on all-cause mortality and adverse events defined as treatment failure, major bleeding and all-cause stroke at day 30 (primary outcome)
- leads to a better Desirability of Outcome Ranking (DOOR) at day 7
- associated with a lower level of oxygen supplementation at 48 hours
- associated with shorter length of stay (LOS) at the intensive care unit (ICU) and in the hospital
- associated with better functional recovery as well as better patient-reported outcomes such as QoL at one year
- cost-effective with a time horizon of one year

Study design

TORPEDO-NL will be an investigator-initiated, academically sponsored, multicentre, open-label, randomized controlled trial (RCT) designed to show superiority of CDT (2 systems; technical variant) on top of regular anticoagulation over systemic thrombolysis plus regular anticoagulation in patients with high-risk PE in the Netherlands. A 2:1 (thrombectomy: systemic thrombolysis) randomization will be applied. The randomization procedure will be web-based, using randomly sized blocks consisting of 3,6 or 9 patients. Randomization will occur after the verification that a thrombectomy procedure can be started (randomization-to-needle time) within 60 minutes. Randomization will be stratified by centre.

Intervention

The intervention consists of immediate thrombectomy without systemic/locally administered thrombolysis.
Thrombectomy is performed via jugular or femoral venous access by an interventional cardiologist, interventional radiologist or vascular surgeon according to the instructions for use (IFU) for the particular device. The catheter is advanced over a preplaced guidewire across the right heart into the pulmonary arteries to the location of proximal thrombus. Procedural therapeutic anticoagulation with heparin is administered. After removal of the dilator, the thrombus is extracted by controlled volume aspiration through an aspiration catheter using a syringe or dedicated aspiration system, with multiple aspirations performed as needed. Procedural objectives will be clearly stated prior to the intervention and patient*s clinical and hemodynamic status and residual thrombus will guide the investigators to

determine when to terminate the procedure. Treatment success is defined as clear evidence of right ventricular recompensation. The procedure must be discontinued in case of treatment failure, i.e. lack of improvement or hemodynamic deterioration, and major CDT complications such as cardiac arrest or severe haemoptysis. Complications will be solved directly, with a procedure/treatment best suitable according to the treating physician, to minimalize the risk of damage and promote patient recovery.

Study burden and risks

Thrombectomy requires a procedure but may in part prevent the bleeding risks associated with systemic thrombolysis. Further, patients will be followed for 1 year and asked to complete a set of patient reported outcome measures several times. Benefit for patients involves a potentially lower mortality and incidence of treatment failure and/or adverse events, lower short-term oxygen requirement, a faster and better relief of functional limitations, a shorter LOS, at the ICU and in-hospital, and better long-term outcomes of care.

Contacts

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Trial sites

Trial sites in the Netherlands

Amphia Ziekenhuis
Target size: 8

Amsterdam UMC

Target size: 8

Isala
Target size: 8

Leids Universitair Medisch Centrum
Target size: 8

Erasmus MC, Universitair Medisch Centrum Rotterdam
Target size: 8

Radboud Universitair Medisch Centrum
Target size: 8

Universitair Medisch Centrum Utrecht
Target size: 8

Rijnstate Ziekenhuis
Target size: 8

Haaglanden Medisch Centrum (HMC)
Target size: 8

HagaZiekenhuis
Target size: 7

Maastricht Universitair Medisch Centrum +
Target size: 8

Maasstadziekenhuis
Target size: 8

Noordwest Ziekenhuisgroep
Target size: 7

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Adult patients with confirmed acute PE, i.e. contrast filling defect in a lobar or more proximal pulmonary artery on computed tomography pulmonary angiography (CTPA), and/or obstructive shock with echocardiographic confirmed dilatation of the right ventricle and a congested vena cava inferior, both

with/without echocardiographic signs of clot in transit or deep vein thrombosis of the leg.

2. High risk for mortality, i.e.
a. post cardiac arrest (after temporary need for cardiopulmonary resuscitation), OR
b. obstructive shock (systolic blood pressure <90 mmHg and signs of end-organ hypoperfusion (e.g. elevated lactate levels >2 mmol/l) or the need for vasopressors (adrenalin or noradrenalin) to maintain an adequate blood pressure), OR
c. persistent hypotension (systolic blood pressure <90 mmHg or systolic blood pressure drop >=40 mmHg for at least 15 minutes) not caused by new onset arrhythmia, hypovolemia, or sepsis, OR
d. abnormal RV function on transthoracic echocardiography or CTPA AND elevated cardiac troponin levels AND respiratory failure defined as hypoxemia (SaO2 <90%) refractory to O2 supplementation by nasal cannula or Venturi mask, requiring full face mask O2 supplementation (100% FiO2), high-flow nasal O2, or (non-)invasive mechanical ventilation.

3. CDT available and technically feasible so as to allow for a randomization-to-needle time of 60 minutes or less.

Exclusion criteria

1. 'Catastrophic PE', i.e. ongoing cardiac arrest and/or need for extracorporeal cardiopulmonary resuscitation (ECPR) and/or immediate indication for venoarterial extracorporeal membrane oxygenation (VA-ECMO) as judged by the responsible physician(s)
2. Glascow Coma Scale <8 following resuscitation for cardiac arrest
3. Alternative diagnosis than acute PE contributing largely to the acute hemodynamic and/or respiratory failure, e.g. sepsis, COPD GOLD 3 or 4, or known heart failure with NYHA Functional Classification of 4, as judged by the treating physician.
4. A known 'do not admit to the ICU' or 'do not resuscitate' directive
5. An absolute contraindication to systemic thrombolysis, i.e.
- History of hemorrhagic stroke
- Ischemic stroke in past 6 months
- Central nervous system neoplasm
- Major trauma, major surgery or major head injury in past 3 weeks (note: mild external laceration of the head after, e.g. syncope, does not count as major head injury, especially when a CT scan of the head shows no hematoma)
- Active bleeding, life-threatening or into a critically organ/area; OR known severe bleeding diathesis with previous bleeding fulfilling these criteria
6. Reperfusion therapy (systemic thrombolysis, surgical thrombectomy or

CDT/other catheter directed therapy), or placement of a non-retrieved inferior vena cava filter for acute pulmonary embolism in the past 3 months
7. Thrombus in transit through a patent foramen ovale.
8. Known chronic thromboembolic pulmonary hypertension (CTEPH), or strong suspicion of CTEPH based on pre-existing clinical findings and combinations of signs of PE chronicity on echocardiography and/or CTPA.
9. Known hypersensitivity to systemic thrombolysis, heparin, or to any of the excipients
10. If, in the Investigator's opinion, or after consultation with the local PERT-team or EC-members, the patient is not appropriate for thrombectomy
11. Chronic use of full-dose oral or parenteral anticoagulation before presentation.
12. Pregnancy
13. Current participation in another study that would interfere with participation in this study
14. Previous enrolment in this study
15. Refusal of deferred consent by the next of kin or by the patient himself to use the data. Deferred consent will not be asked to relatives of patients who die in scene, but are included in the study.

Study design

Design

Study phase:	N/A
Study type:	Interventional research previously applied in human subjects
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Other type of control
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	31-03-2025
Enrollment:	111
Duration:	12 months (per patient)

Type:	Actual

Medical products/devices used

Product type:	Medical device
Generic name:	Catheter
Registration:	Yes - CE intended use

IPD sharing statement

Plan to share IPD: Yes

Plan description
N.a.

Ethics review

Approved WMO Date:	23-12-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	22-04-2025
Application type:	Amendment
Review commission:	METC LDD

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ClinicalTrials.gov	NCT06833827
CCMO	NL87503.058.24
Research portal	NL-005298